

DYSFUNCTIONAL UTERINE BLEEDING

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DEFINITIONS:

Dysfunctional Uterine Bleeding (DUB): excessive, prolonged, or irregular uterine bleeding in a reproductive aged woman who lacks pelvic organ disease or a systemic disorder.

Menorrhagia: excessive uterine bleeding occurring at the regular intervals of menstruation, the period of flow being greater than usual in duration

Metrorrhagia: uterine bleeding of a normal amount, occurring at completely irregular intervals

Menometrorrhagia: excessive uterine bleeding occurring both during the menses and at irregular intervals

Oligomenorrhea: markedly diminished menstrual flow; relative amenorrhea; infrequent menstruation

Hypermenorrhea: excessive uterine bleeding occurring at regular intervals, the period of flow being of usual duration

Hypomenorrhea: uterine bleeding of less than normal amount occurring at regular intervals, the period of flow being of the same or less than usual duration

GENERAL CONSIDERATIONS

- 10-15% of pts referred to gynecologists are treated for DUB. Half of these are perimenopausal; 20% are perimenarchal and the rest are in the reproductive age group
- Most cases of DUB are associated with ovulatory dysfunction.
- You MUST make the correct dx to rx properly!

THE NORMAL MENSTRUAL CYCLE

- The normal menstrual cycle is a result of complex interaction between hypothalamus, anterior pituitary, ovary and endometrium.
- Maturation of the endometrium is relatively uncomplicated (compared with the maturation of the oocyte) and is solely dependent upon two hormones, estrogen and progesterone.
- The first half of the menstrual cycle (proliferative phase) is estrogen dependent resulting in growth of the endometrium from 1 to 5 mm at the time of ovulation.
- The second half of the menstrual cycle (secretory phase) is progesterone dominant. Progesterone halts the growth of the endometrium and stimulates secretory activity in the endometrium.
- Menstruation occurs when both progesterone and estrogen levels fall after the failure of conception. Synchronous shedding of the endometrial lining occurs.
- ****Note** Random breakdown of the endometrial lining (DUB) does NOT occur when the endometrium has been adequately primed with estrogen and stabilized with progesterone.**

Normal menses:

- Last 2-7 days
- Blood loss ranges from 25-70 ml (average 30-35ml)
- Mean cycle length is 29 days (range 21-40 days)

EVALUATION OF ABNORMAL UTERINE BLEEDING

1. First decide if this is really abnormal bleeding and is an evaluation justified? Isolated events may not be worth pursuing.
2. It is nearly impossible to estimate blood loss from history. Clotting or bleeding > 7 days suggest substantial blood loss but the only objective way to quantitate blood loss is by checking a CBC. Hct < 30 implies significant blood loss.

**** Bleeding at a rate of soaking a tampon or pad in an hour for at least 2 consecutive hours implies PROFUSE bleeding. Orthostatic hypotension implies hemodynamic instability. Urgent evaluation is imperative!!**

3. The coloration of the blood can often give clues to the etiology of the abnormal bleeding. Brown or prune-colored discharge superimposed upon regular red menstrual bleeding is most commonly caused by an **obstructed genital tract**. It may be heavy, initially continuous, and most often will be noted immediately after a menstrual period. **Endometriosis** also causes brown discharge but this is usually premenstrual. Cervical endometriosis and stenosis trap blood within the endometrial cavity. As the cervix dilates late in the cycle, the trapped old blood and by-products are allowed to empty from the cavity.

4. Next decide if the bleeding is **ovulatory** or **anovulatory**.

Ovulatory bleeding: Bleeding which occurs at regular intervals and is preceded by premenstrual symptoms:

- Breast tenderness
- Water weight gain
- Mood swings
- Abdominal cramping

Anovulatory bleeding: prolonged bleeding occurring at irregular intervals followed by months of amenorrhea

5. To determine if the woman is ovulating, it may help to:
- Do Basal Body Temperature determinations (ovulation should increase body temperature by half a degree or so during the last 2 weeks of the cycle).
 - Perform ovulation predictor tests
 - Measure progesterone levels (>9.5 nmol/li or > 3 ng/ml is evidence that ovulation has taken place)
 - Endometrial biopsy showing secretory changes confirms ovulation

OVULATORY DUB

Ovulatory bleeding is more likely to be associated with an **anatomic** or **organic** cause such as fibroids, infections, lacerations, or polyps.

- **Pregnancy-related causes of DUB:**
- Ectopic pregnancy
- Spontaneous abortion
- Incomplete abortion
- Threatened abortion

- Retained products of conception
- Placental products
- Trauma at delivery
- Trophoblastic disease
- **Inflammatory causes of DUB:**
- Endometritis: prolongation of normally timed menses or irregular spotting
- Cervicitis: prolongation of normally timed menses or irregular spotting
- Vaginitis: infection with *Trichomonas* can cause persistent spotting superimposed upon normal cyclic bleeding
- IUD: prolonged heavy bleeding during normally timed menses
- Foreign body: retained tampon or diaphragm results in irregular spotting usually of old blood
- Lacerations

- **Systemic Diseases which cause DUB:**
- Blood dyscrasias (ITP, Von Willebrand's): Pts with Von Willebrand's may have normal PT, PTT but abnormal bleeding times. Von Willebrand's disease is the most common inherited clotting disorder that can present at menarche as severe menorrhagia.
- Malnutrition
- Anticoagulant therapy
- Thyroid disease

- **Tumors which cause DUB:**
- Fibroids: submucous myomata are notorious for causing prolonged heavy bleeding; common in older women and in African Americans. Submucous fibroids are not obvious on exam (try endovaginal ultrasound)
- Adenomyosis
- Endometriosis: most commonly presents with luteal phase spotting characterized by dark brown or prune colored discharge
- Polyps
 - Cervical: often post-coital spotting
 - Uterine: may present with prolonged trail-off spotting at the conclusion of a normally timed menses or persistent spotting throughout the cycle

- Endometrial hyperplasia
- Cervical hemangiomas: very heavy bleeding, often after trauma
- Cancer of the cervix, endometrium, or fallopian tubes

ANOVULATORY DUB

- Anovulatory DUB can be secondary to chronic unopposed estrogen or estrogen withdrawal
 - In chronic unopposed estrogen states, the endometrium is continuously stimulated by estrogen which causes proliferation without the stabilization from progesterone. The endometrium sloughs in an irregular and incomplete manner. Areas that have shed begin to heal under the influence of continuous estrogen. This random, non-uniform shedding/healing can cause profuse and prolonged bleeding.
 - In estrogen withdrawal states, estrogen levels may rise but insufficiently to trigger an LH surge. Bleeding occurs when estrogen levels fall.
- There are both **physiologic** and **pathologic** causes of anovulatory bleeding.

Physiologic Causes:

1. **Puberty:** The first cycles after menarche are anovulatory and the bleeding is secondary to estrogen withdrawal. This bleeding is usually light to moderate and occurs at 22-45 d intervals.
2. **Perimenopausal:** The peak estrogen level attained as a woman nears menopause will not be sufficient to trigger an LH surge and ovulation fails. Bleeding occurs because of estrogen withdrawal.

Pathologic Causes: Dysfunction can occur at any level of the hypothalamic-pituitary-ovarian axis.

1. **Ovarian Failure:** can be premature and associated with an autoimmune process
2. **Hypothalamic amenorrhea:** can be from weight loss, emotional stress or chronic illness
3. **Polycystic Ovary Syndrome:** associated with obesity, hirsutism, infertility and anovulatory DUB
4. **Other causes:** hyperprolactinemia

EVALUATION OF DUB

1. History:

- ?frequency and amount of blood flow (**Remember** Soaking 1 pad or tampon in an hour for at least 2 hours constitutes worrisome flow)
- ?dysmenorrhea
- ?bruising
- ?epistaxis
- ?gingival bleeding
- ?perimenopausal symptoms
- ?sexual behaviors

2. Physical examination:

- Check orthostatics
- ?pale conjunctiva
- ?cervical polyp
- ?enlarged uterus

3. Labs:

- CBC (stat, if indicated)
- hCG
- Pap smear
- Chlamydia
- Gonorrhea

4. As indicated:

Endovaginal ultrasound

- Peripheral smear
- Coagulation profile (plt, PT, PTT, bleeding time)
- TFTs, prolactin, LH, FSH
- Wet preps
- Endometrial biopsy:
 - Age 35
 - Clinical suspicion of prolonged unopposed estrogen state (PCOS, iatrogenic unopposed estrogen)

MANAGEMENT OF DUB

1. The approach to stopping the initial bleeding depends upon the severity. For **acute profuse bleeding**:
 1. Consult gynecology
 2. If the patient is hemodynamically stable:
 - a. oral contraceptives:
 2. 1 tablet qid for 5-7 days. Flow should cease within 12-24 hours. Within 2-4 days of stopping therapy, the pt should experience heavy, crampy flow. On the fifth day of flow, start a low dose OC daily for at least three 28 day cycles along with FeSO₄ supplementation
 3. Alternatively, 1 tablet qid until bleeding stops. Begin FeSO₄. Once bleeding stops, taper pills by taking 1 pill q 8 hrs x 3 d; then 1 pill q 12 hrs x 3 d; then 1 pill daily to complete the 21 day cycle. Cycle on low dose OC's for 3-6 months. With each successive cycle, the pt's bleeding should become lighter and shorter.
 4. Alternatively, to avoid a withdrawal bleed immediately after stopping DUB, use a 21-day monophasic pill packet or a 28-day pill packet with the 7 placebo pills removed to stop acute bleeding as above. When the initial packet is empty, immediately begin a new 28-day packet of at least 35 microgram pills. Warn the pt that the first menses on this packet is likely to be heavy because of endometrial thickening in response to the estrogen. It will lighten over the subsequent months. She should stay on the OC's at least another 3 months.
 3. If the patient is not hemodynamically stable: refer to gyn for IV premarin or D&C.

For chronic DUB, the approach depends upon your best judgment about whether the patient is **ovulatory** or **anovulatory** and the cause of the DUB:

- Medroxyprogesterone acetate and megestrol acetate are effective oral progestational agents which can be used to stop **anovulatory** bleeding. Medroxyprogesterone acetate (Provera) can be given at 10-40 mg/d in divided doses and continued for 5-10 d. This approach works well in patients in whom there is sufficient endometrium remaining to allow progestin induced stabilization. Long-term therapy can be accomplished with cyclical progestins (10 mg Provera daily for 14 days/month).
- Again, for **anovulatory** bleeding, since all oral contraceptives are progesterone-dominant, any low dose monophasic oral contraceptive can be administered at a dose of 1-4 pills per day and continued for 1 week and then decreased to one pill a day. Bleeding should slow or stop within 24-48 hours of starting the OC; if not, further investigation is warranted. The estrogen provides the benefit of a growth and healing effect on the endometrium so that progesterone will have its maximal effect. OC's may be continued for 3-6 months.

- Progesterone alone has proven useful in management of DUB associated with **fibroids**. DepoProvera injections completely atrophy the endometrium and thus stop bleeding.
- Estrogen alone also has a role in the treatment of DUB. Long term treatment with oral contraceptives or progestational agents such as Norplant or DepoProvera result in atrophic changes in the endometrium that make it prone to bleeding. Resolution of this bleeding can be achieved by adding 10-20 ug of ethinyl estradiol or 1.25 to 2.5 mg conjugated estrogen for 10 d to 3 months.
- Cyclic NSAID's will reduce the amount of flow during regularly timed menses and will also relieve cramps. Advise the patient to begin NSAID 1-2 days before their menses and continue regular doses of the NSAID throughout the menses.
- Begin iron therapy and continue for 3-6 months while monitoring Hct.

INDIVIDUALIZED APPROACH TO TREATMENT OF DUB

Adolescent:

- Anovulatory bleeding after menarche is common.
- If the bleeding is not significant, then observation alone is sufficient
- Rule out pregnancy, even in the adolescent who denies sexual activity
- Adolescents who present with heavy vaginal bleeding after several months of amenorrhea are best treated with OC's. Treatment can be stopped after 3-6 months to see if a normal menstrual cycle has been established.

Acute Anovulation:

- Most women with normal menstrual cycles will occasionally have an anovulatory cycle that can result in protracted bleeding.
- Rule out pregnancy first and then treat with a single course of a progestational agent such as 10 mg Provera for 5-10 d. If the bleeding does not resolve in 48-72 hours, then you must rule out another cause of the bleeding

Chronic Anovulation:

- Monthly administration of a progestational agent will result in regular endometrial shedding which will protect against endometrial cancer.
- A 12 day course of medroxyprogesterone at 10 mg/d should be adequate.
- If occasional ovulation cannot be ruled out and the woman does not desire pregnancy, then oral contraceptives are a better choice.
- Any woman with at least a 1 year history of anovulation should be referred to a gynecologist for endometrial biopsy

Perimenopausal Women:

- Many perimenopausal women fluctuate between ovulatory and anovulatory cycles.
- Low dose oral contraceptives can be used to provide a monthly withdrawal bleed and provide contraception as well.
- The FDA has approved use of oral contraceptives in women up to the time of menopause as long as there is no contraindication such as smoking, HTN, clotting disorders or hyperlipidemia.
- To determine that a woman has entered menopause, an FSH > 40 on day 6 or 7 of the placebo pills confirms ovarian failure and the pt can then be switched to hormone replacement therapy.

OTHER MANAGEMENT OPTIONS

Most cases of DUB can be managed medically but occasionally hysteroscopy and/or D & C may be necessary. Endometrial ablation is an alternative to hysterectomy and is effective in > 50% of cases.

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